EDITORIAL

The value of rhythm control in mitral stenosis

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The haemodynamic consequences of atrial fibrillation in patients with mitral stenosis have received little attention despite their clinical significance. What role does rhythm control have in the treatment of these patients?

It is well recognised that patients with mitral stenosis (MS) and atrial fibrillation (AF) face a substantial risk of systemic thromboembolism. Anticoagulation with vitamin K antagonists partially offsets this risk.[1] However, because of our preoccupation with non-valvular AF, the haemodynamic consequences of AF in patients with MS[2] have received little attention in recent times. The article by Hu and colleagues,[3] in this issue of *Heart*, presents an opportunity to review the value of sinus rhythm (SR) in the haemodynamics of MS.

Clinical deterioration with the onset of AF occurs because of the loss of atrial contraction and increase in heart rate, resulting in reduced cardiac output and functional capacity.[2] Symptom status, exercise capacity and quality of life all improve with conversion to SR.[2 4] While the detrimental effects of the reduction in diastolic filling time with increase in heart rate are well understood, the role of the loss of atrial systole is not as clear.

ATRIAL CONTRIBUTION TO VENTRICULAR FILLING IN MITRAL STENOSIS

Normally, most of the ventricular filling occurs during early diastole, independent of atrial contraction. Atrial contraction contributes to no more than a quarter of the ventricular inflow during SR in normal, young individuals. This proportion rises to about 40% with increasing age and impairment of ventricular relaxation.[5] Ventricular filling differs in three important ways in the presence of MS (figs 1 and 2). Firstly, early peak mitral flow is reduced despite increases in left atrial (LA) pressure and flow velocities. Secondly, the rate of deceleration of transmitral flow is reduced, concomitantly reducing the rate of fall of the atrioventricular pressure gradient. As a result, in contrast to the normal situation where ventricular filling is complete in early diastole, it is prolonged in proportion to the severity of mitral obstruction (measured as the pressure half-time on the mitral inflow Doppler). And finally, the increase in transmitral flow caused by atrial contraction is blunted despite the increase in LA pressure and flow velocity. In short, there is a pan-diastolic derangement of ventricular filling in MS. In the presence of reduced peak mitral flow in early diastole, it would appear that the contribution of atrial systole to ventricular filling would be substantial in MS. However, there is a surprising amount of controversy in the literature regarding this assumption. Studies have varyingly reported that atrial contribution to ventricular filling in MS is more than, about the same as, or less than that in the normal heart.[6–8]

There are several explanations for these discrepant observations. Given the complexity of the ventricular filling abnormality, teasing out the contribution of atrial contraction and accurately measuring it is a difficult proposition. The early studies were performed in the late 1960s and early 1970s, and estimated ventricular filling using indirect, inherently inaccurate indices like cineangiograms, and atrioventricular pressure gradients.[6 8] More recently, studies have employed less indirect measures like Doppler derived estimates of flow.[9 10] Indirect approximations of ventricular filling account for part of the inconsistency between published studies. Another important difference is the failure of some investigators to distinguish atrial conduit and reservoir functions from the ''booster-pump'' function, which is the point of interest. Furthermore, few studies have been able to determine the contribution of atrial contraction, independent of changes in diastolic filling time with varying heart rates.

Nevertheless, a few broad conclusions can be drawn from the available literature:

- Atrial fibrillation in MS is associated with elevated LA pressures and transmitral gradients, larger LAs and a lower cardiac output.[7 8]
- Changes in ventricular rate and the loss of atrial contraction both contribute to the reduced ventricular filling (and resultant reduction in cardiac output) in AF.[7 8]
- Atrial contribution to ventricular filling in severe MS is *less* than that in normal individuals.[8]

The last conclusion appears counterintuitive and has led some authors to erroneously underestimate the importance of the loss of atrial pump function with the onset of AF. Reduction in atrial contribution in patients with MS in SR is *despite* forceful atrial contractions and is a result of increased resistance to flow across the mitral valve. Phylogenetically, the left atrium is intended primarily as a reservoir and conduit rather than as a contractile chamber, and is incapable of overcoming the resistance offered by

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Abbreviations: AF, atrial fibrillation; LA, left atrial; MS, mitral stenosis; PTMC, percutaneous transvenous mitral commissurotomy; SR, sinus rhythm

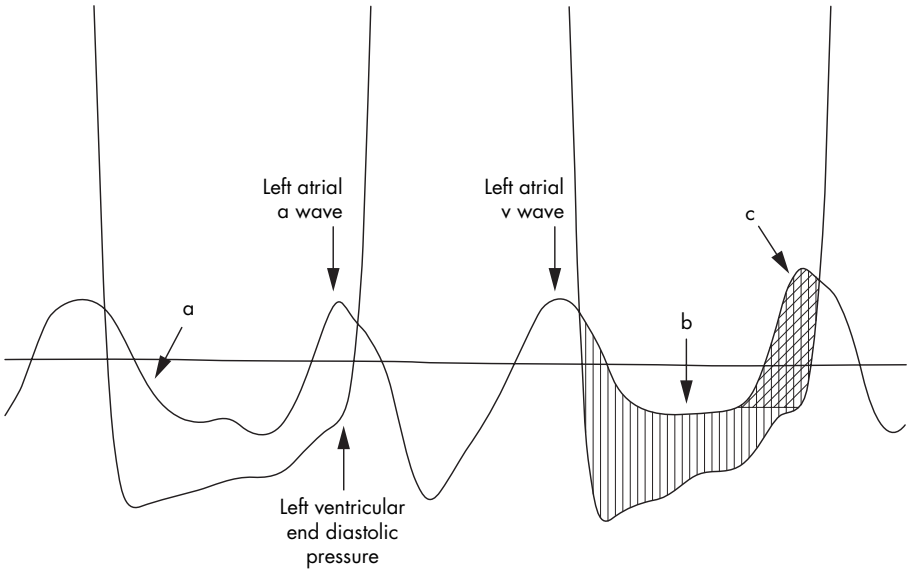


Figure 1 Simultaneously recorded left ventricular and left atrial pressures in a patient with severe mitral stenosis, showing the derangement in ventricular filling. a: elevated left atrial pressure and transmitral gradient during early ventricular filling; b: reduced rate of fall of left atrial pressure and atrioventricular pressure gradient; c: elevated left atrial pressure and transmitral gradient during atrial systole. Vertically hatched area: transmitral gradient responsible for flow independent of atrial contraction. Crosshatched area: rise in transmitral gradient produced by atrial systole, which drives end diastolic ventricular filling (atrial contribution) (also see fig 2).

a severely stenosed mitral valve. Meisner and colleagues[8] showed in a computer model that enhanced atrial contraction could completely restore atrial contribution to normal at low mitral resistances, but not at higher resistances. They also demonstrated that the fraction of ventricular filling contributed by atrial contraction was greatest (about 29%) in patients with mild MS and least (about 9%) in those with severe MS. Most pertinently, it has been shown that reducing valve resistance by percutaneous valvotomy restores atrial contribution to normal.[9 10] However, advancing age impairs the recovery of atrial contractile function after valvuloplasty.[9]

Therefore, in patients with MS, atrial contribution remains a potential resource to improve cardiac output, and can be recruited by early intervention to open the mitral valve, combined with a strategy to restore and maintain SR (fig 2).

RESTORATION AND MAINTENANCE OF SINUS RHYTHM IN MITRAL STENOSIS

Arguably, the most important proximate cause of AF in MS is LA stretch caused by raised LA pressure. In addition to reducing LA pressure, percutaneous transvenous mitral commissurotomy (PTMC) has been shown to favourably alter atrial refractoriness[11] and conceivably set the stage for reversion to SR. However, most patients in chronic AF before PTMC fail to revert to SR in the absence of an aggressive antiarrhythmic strategy.[12–14] Furthermore, only a few of the patients who do revert remain in SR at follow-up.[12] Therefore, combining PTMC with an aggressive antiarrhythmic strategy offers the best prospect of rhythm control. This has previously been attempted, in non-randomised studies, with favourable results. Duration of AF, LA size, and age are the principal determinants of successful cardioversion and maintenance of SR.[13 14]

Hu and colleagues report the results of the first randomised controlled trial of a rate versus rhythm control strategy immediately following PTMC.[3] The authors report remarkable success with a rhythm control strategy (96% of the patients were in SR at one year) with concomitant improvements in symptom status, exercise capacity, and quality of life. The large patient number and the randomised design lend credence to these conclusions. As a study addressing an issue of major public health concern in much of the developing world, it is a welcome addition to the sparse literature on the subject. Nonetheless, several aspects of the study warrant comment.

Patient selection and study end point

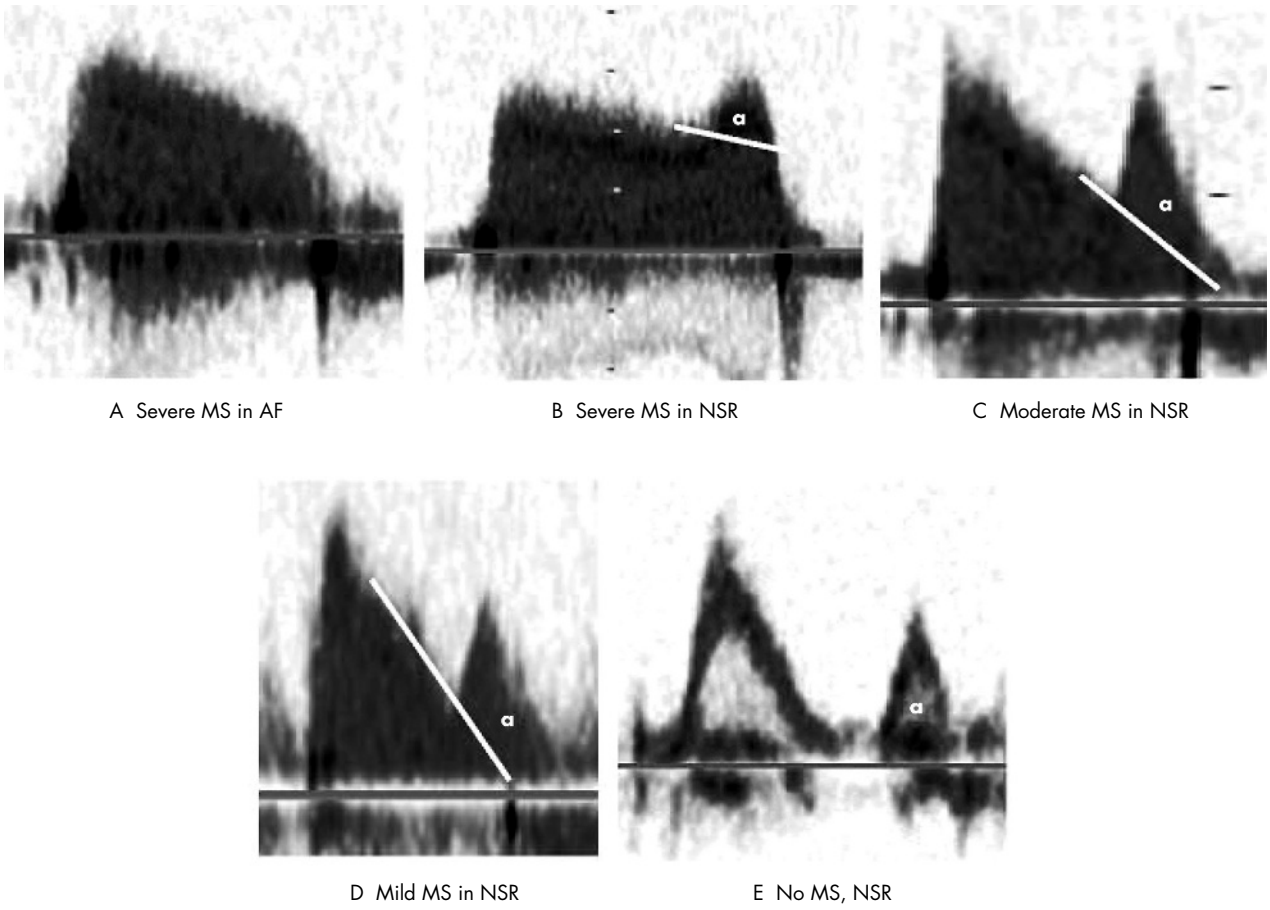
It is surprising that the authors chose to use ''atrial fibrillation-related symptoms'' as the primary outcome measure driving the sample size calculations. Clearly, in patients with MS (albeit mild), and possibly other coexistent valvular disease, the occurrence of palpitations, ''episodes of dyspnoea'', and ''dizzy spells'' cannot be reasonably attributed to AF alone! Further, this would not have been a representative end point, if a significant proportion of patients in the rhythm control group had remained in AF. Considering the difficulty of achieving and maintaining SR in this difficult patient subset, successful cardioversion and maintenance of SR are arguably the points of greatest interest. Fortunately, the rhythm control strategy turned out to be successful enough to be convincing.

The authors do not provide any information about how patients were randomised and, more importantly, if treatment allocation was adequately concealed. In an open label trial, allocation concealment is of crucial importance in order to avoid selection bias, which can undermine the process of randomisation. Further, it is not clear from the article whether patient interviews were conducted by physicians unaware of the treatment allocation. In studies involving subjective end points, the need for a blinded assessment of outcomes cannot be overemphasised.

It should be noted that these results apply to a highly selected population (LA diameter $\leqslant$ 45 mm; AF duration $\leqslant$ 12 months). Earlier studies including higher risk patients were not as successful with rhythm control.[4 13 14] In order to place the results of this study in perspective, it would have been useful to know the proportion of patients who were excluded and the reasons for their exclusion.

Antiarrhythmic strategy and treatment in the control group

While other investigators performed DC cardioversion 6–8 weeks after starting oral amiodarone, [4 13 14] Hu and colleagues chose to perform DC cardioversion one week after beginning oral dosing. Given the large volume of distribution and the prolonged elimination half-life of amiodarone, steady state concentrations are unlikely to have been achieved in a week. Surprisingly, however, the rate of restoration of SR was not very different from the previous studies. It is possible that, as in ventricular fibrillation, cardioversion might be facilitated early after amiodarone administration.



A Severe MS in AF B Severe MS in NSR C Moderate MS in NSR

D Mild MS in NSR E No MS, NSR

Figure 2 Mitral inflow Doppler recordings illustrating the importance of sinus rhythm and an open mitral valve in ventricular filling. Panel A: No atrial contribution in severe mitral stenosis (MS) in atrial fibrillation (AF). Panels B to E: Increasing proportion of ventricular filling from atrial contraction (a, area above and to the right of the white lines) with larger mitral valve areas. NSR, normal sinus rhythm.

It appears that close to 60% of patients received digoxin for rate control and about 70% received two drugs. However, we are not provided details of the drugs used or the dosages in which they were used. More importantly, the authors do not provide any details of the actual heart rate control achieved. It is unclear how they ensured that heart rate was within the prespecified 90–115/min during ''moderate exercise''. Outcomes related to functional capacity are bound to be affected by the degree of rate control achieved.

Clinical implications

Should rhythm control be the strategy of choice in patients with MS and small LAs, who have been in AF for less than a year? There is not as much doubt about the strategy as there is about the means adopted to control rhythm. Initiating long term (possibly lifelong) amiodarone treatment in young individuals exposes them to the risk of potentially lethal side effects. Although low dose amiodarone (< 200 mg/day) might be relatively safe in western populations,[15] 200 mg/day might not be ''low-dose'' for the typical, small built, undernourished patient with MS. Evidence of safety at long term follow-up in this population is needed, before this strategy can be universally advocated. Dronedarone, an amiodarone analogue, holds promise of similar efficacy, without the non-cardiac side effects. Class IC agents are likely to be safe in this situation (young patients, low likelihood of coronary artery disease, and normal left ventricular function) and need to be tested. Alternative paradigms of AF induction and sustenance should be explored and may point the way to new treatments in the future.[16] For now, effective rate control with adequate anticoagulation continues to remain an acceptable option.

Competing interests: None

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IMAGES IN CARDIOLOGY

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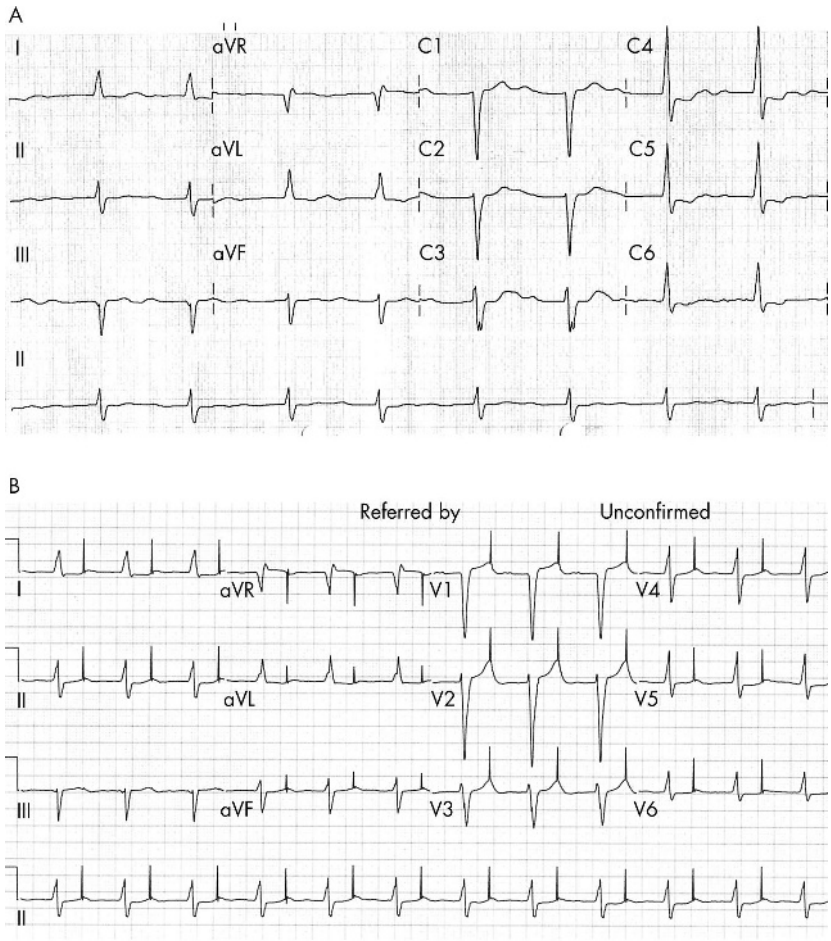
Abnormal ECG following insertion of a temporary pacing wire

A 90-year-old man was referred for insertion of a permanent pacemaker system. He had been admitted to a local hospital with an episode of sinus arrest with escape ventricular tachycardia and ventricular fibrillation. An earlier ECG had shown sinus rhythm with pronounced first degree atrioventricular block (panel A). He was successfully resuscitated and a transvenous temporary pacing wire was inserted via the right internal jugular vein. It was commented on at the time that ''position of the wire not perfect, but pacing!''

His ECG showed a paced rhythm of 70 beats/min with complete left bundle branch block morphology, atrial pacing spikes with prolonged atrioventricular delay, and left axis deviation (panel B). He was cardiovascularly stable with no further documented rhythm disturbances and a blood pressure of 180/90 mm Hg. The threshold of the temporary pacing wire was high at 3 volts.

On fluoroscopy the temporary pacing wire was found to be positioned on the outer border of the cardiac silhouette, arcing round the posterior surface of the heart which was pacing the high lateral region of the left atrium (panel C, arrow). A dual chamber pacing system was inserted. Removal of the temporary wire, with immediate echocardiographic assessment for pericardial accumulation, was uneventful.

Malposition of pacing leads through the coronary sinus, patent foramen ovale or through the arterial system into the left ventricle are recognised complications of lead insertion. However, right ventricular perforation and subsequent atrial epicardial pacing has not been reported in haemodynamically stable patients.



Temporary pacing wires should be avoided unless essential. Complication rates remain high due to a combination of the stiffness of the catheters, and relatively junior inexperienced operators.

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